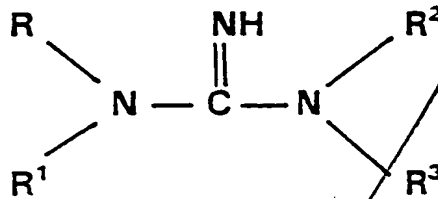


What is claimed is:

1. A compound of the following formula I:

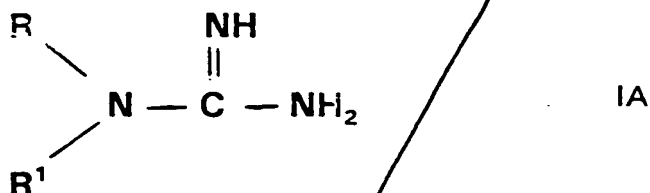


wherein:

R and R<sup>1</sup> are each independently substituted or unsubstituted alkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkoxy having from 1 to about 20 carbon atoms, substituted or unsubstituted aminoalkyl having 1 to about 20 carbon atoms, substituted or unsubstituted alkylthio having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfinyl having from 1 to about 20 carbon atoms, substituted or unsubstituted carbocyclic aryl having at least about 5 ring atoms, substituted or unsubstituted aralkyl having at least about 5 ring atoms, or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having from 1 to 3 rings, 3 to 8 ring members in each ring and from 1 to 3 hetero atoms, with at least one of R and R<sup>1</sup> being carbocyclic aryl, aralkyl, or a heteroaromatic group or heteroalicyclic group;

R<sup>2</sup> and R<sup>3</sup> each being independently selected from the group consisting of hydrogen, substituted and unsubstituted alkyl, substituted and unsubstituted alkoxy, substituted and unsubstituted thioalkyl, and substituted and unsubstituted aminoalkyl; and wherein said compound exhibits high inhibition of glutamate release; and pharmaceutically acceptable salts thereof.

2. A compound having the following Formula IA:



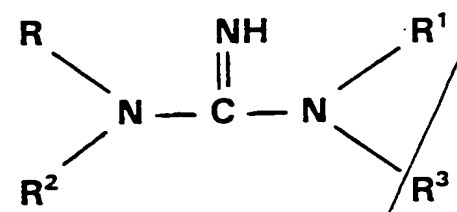
wherein R and R<sup>1</sup> are each independently substituted or unsubstituted alkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms, substituted or unsubstituted carbocyclic aryl having at least about 5 ring atoms, substituted or unsubstituted alkoxy having from 1 to about 20 carbon atoms, substituted or unsubstituted aminoalkyl having 1 to about 20 carbon atoms, substituted or unsubstituted alkylthio having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfinyl having from 1 to about 20 carbon atoms, substituted or unsubstituted aralkyl having at least about 5 ring atoms, or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having from 1 to 3 rings, 3 to 8 ring members in each ring and from 1 to 3 hetero atoms; and pharmaceutically acceptable salts thereof.

3. A compound of claim 2 wherein at least one of R and R<sup>1</sup> is substituted or unsubstituted carbocyclic aryl or substituted or unsubstituted aralkyl.

4. A compound of claim 2 selected from the group of:
- N-(4-*sec*-butylphenyl)-N-benzylguanidine;
  - N-(5-acenaphthyl)-N-benzylguanidine;
  - N-(3-acenaphthyl)-N-benzylguanidine;
  - N-(5-acenaphthyl)-N-(4-*isopropylbenzyl*)guanidine;
  - N-(3-acenaphthyl)-N-(4-*isopropylbenzyl*)guanidine;

N-(4-cyclohexylphenyl)-N-(4-isopropylbenzyl)guanidine;  
N-(4-cyclohexylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(2-fluorenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(4-*sec*-butylphenyl)-N-(cinnamylmethylene)guanidine;  
N-(4-*n*-butoxyphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-biphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(5-indanyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-trifluoromethoxyphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(4-*sec*-butylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(5-acenaphthyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-acenaphthyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(methoxy-1-naphthyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(1-naphthyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-iodophenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(4-chloro-1-naphthyl)-N-(4-*tert*-benzyl)guanidine;  
N-(4-*tert*-butylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(4-iodophenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(1-naphthylmethyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(5-acenaphthyl)-N-(3-phenoxybenzyl)guanidine;  
N-(3-trifluoromethylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-methylthiophenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(5-acenaphthyl)-N-(3-iodobenzyl)guanidine;  
N-(5-acenaphthyl)-N-(cinnamyl)guanidine;  
N-(5-acenaphthyl)-N-(4-iodobenzyl)guanidine;  
N-(5-acenaphthyl)-N-(4-trifluoromethoxybenzyl)guanidine;  
and pharmaceutically acceptable salts thereof.

✓



wherein

R is selected from the group of fluorenyl, phenanthracenyl, anthracenyl and fluoranthenyl;

**R<sup>1</sup> is substituted or unsubstituted alkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkoxy having from 1 to about 20 carbon atoms, substituted or unsubstituted aminoalkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylthio having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfinyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfonyl having from 1 to about 20 carbon atoms, substituted or unsubstituted carbocyclic aryl having at least about 5 ring atoms, substituted or unsubstituted aralkyl having at least about 5 ring atoms, or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having 1 to 3 rings, 3 to 8 ring members in each ring and 1 to 3 heteroatoms;**

R<sup>2</sup> and R<sup>3</sup> are each independently hydrogen or a group as defined for R<sup>1</sup> above; and pharmaceutically acceptable salts thereof.

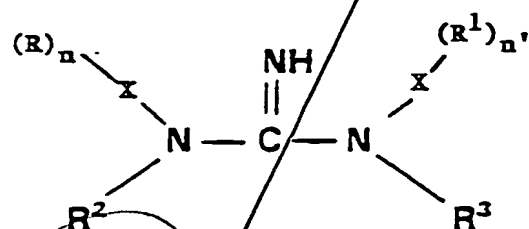
6. A compound of claim 5 wherein R<sup>1</sup> is substituted or unsubstituted carbocyclic aryl.

7. A compound of claim 5 selected from the group of:  
N,N'-bis(2-fluorenyl)guanidine;  
N,N'-bis(2-fluorenyl)-N-methylguanidine;

N,N'-bis(2-fluorenyl)-N,N'-dimethylguanidine;  
N,N'-bis(anthracenyl)guanidine;  
N,N'-bis(anthracenyl)-N-methylguanidine;  
N,N'-bis(anthracenyl)-N,N'-dimethylguanidine;  
N,N'-bis(phenanthracenyl)guanidine;  
N,N'-bis(phenanthracenyl)-N-methylguanidine;  
N,N'-bis(phenanthracenyl)-N,N'-dimethylguanidine;  
N,N'-bis(fluoranthenyl)guanidine;  
N,N'-bis(fluoroanthenyl)-N-methylguanidine;  
N,N'-bis(fluoroanthenyl)-N,N'-dimethylguanidine;  
N-(anthracenyl)-N'-(1-adamantyl)guanidine;  
N-(anthracenyl)-N'-(1-adamantyl)-N-methylguanidine;  
N-(anthracenyl)-N'-(1-adamantyl)-N'-methylguanidine;  
N-(anthracenyl)-N'-(1-adamantyl)-N,N'-dimethylguanidine;  
N-(anthracenyl)-N'-(2-adamantyl)guanidine;  
N-(anthracenyl)-N'-(2-adamantyl)-N-methylguanidine;  
N-(anthracenyl)-N'-(2-adamantyl)-N'-methylguanidine;  
N-(anthracenyl)-N'-(2-adamantyl)-N,N'-dimethylguanidine;  
N-(phenanthracenyl)-N'-(1-adamantyl)guanidine;  
N-(phenanthracenyl)-N'-(1-adamantyl)-N-methylguanidine;  
N-(phenanthracenyl)-N'-(1-adamantyl)-N'-methylguanidine;  
N-(phenanthracenyl)-N'-(1-adamantyl)-N,N'-dimethylguanidine;  
N-(phenanthracenyl)-N'-(2-adamantyl)guanidine;  
N-(phenanthracenyl)-N'-(2-adamantyl)-N-methylguanidine;  
N-(phenanthracenyl)-N'-(2-adamantyl)-N'-methylguanidine;  
N-(phenanthracenyl)-N'-(2-adamantyl)-N,N'-dimethylguanidine;  
N-(fluorenyl)-N'-(1-adamantyl)guanidine;  
N-(fluorenyl)-N'-(1-adamantyl)-N-methylguanidine;  
N-(fluorenyl)-N'-(1-adamantyl)-N'-methylguanidine;  
N-(fluorenyl)-N'-(1-adamantyl)-N,N'-dimethylguanidine;  
N-(fluorenyl)-N'-(2-adamantyl)guanidine;

N-(fluorenyl)-N'-(2-adamantyl)-N-methylguanidine;  
 N-(fluorenyl)-N'-(2-adamantyl)-N'-methylguanidine;  
 N-(fluorenyl)-N'-(2-adamantyl)-N,N'-dimethylguanidine;  
 and pharmaceutically acceptable salts of said compounds.

8. A compound of the following Formula III:



III

wherein

R and R<sup>1</sup> are each independently substituted or unsubstituted alkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkoxy having from 1 to about 20 carbon atoms, substituted or unsubstituted aryloxy having from 6 to about 20 carbon atoms, substituted or unsubstituted aralkoxy having from 6 to about 20 carbon atoms, substituted or unsubstituted aminoalkyl having 1 to about 20 carbon atoms, substituted or unsubstituted alkylthio having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfinyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfonyl having 1 to about 20 carbon atoms, substituted or unsubstituted carbocyclic aryl having at least 5 ring atoms, substituted or unsubstituted aralkyl having at least 5 ring atoms, or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having 1 to 3 rings, 3 to 8 ring members in each ring and 1 to 3 heteroatoms;

R<sup>2</sup> and R<sup>3</sup> are each independently hydrogen or a group as defined for R and R<sup>1</sup> above; or R<sup>1</sup> and R<sup>3</sup> together form a ring having 5 or more ring members;

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X and X' are each independently a chemical bond, substituted or unsubstituted alkylene having from 1 to about 8 carbon atoms, substituted or unsubstituted alkenylene having from 2 to about 8 carbon atoms, or substituted or unsubstituted alkynylene having from 2 to about 8 carbon atoms, substituted or unsubstituted heteroalkylene having from 1 to about 8 carbon atoms, substituted or unsubstituted heteroalkenylene having from 2 to about 8 carbon atoms, or substituted or unsubstituted heteroalkynylene having from 2 to about 8 carbon atoms, with at least one X and X' being other than a chemical bond; and wherein said compound exhibits high inhibition of glutamate release; and pharmaceutically acceptable salts thereof.

- R1N(R2)C(=N)N(R3)R4

wherein

R and R<sup>1</sup> are each independently substituted or unsubstituted alkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkoxy having from 1 to about 20 carbon atoms, substituted or unsubstituted aryloxy having from 6 to about 20 carbon atoms, substituted or unsubstituted aralkoxy having from 6 to about 20 carbon atoms, substituted or unsubstituted aminoalkyl having 1 to about 20 carbon atoms, substituted or unsubstituted alkylthio having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfinyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfonyl having 1

to about 20 carbon atoms, substituted or unsubstituted carbocyclic/aryl having at least 5 ring atoms, substituted or unsubstituted aralkyl having at least 5 ring atoms, or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having 1 to 3 rings, 3 to 8 ring members in each ring and 1 to 3 heteroatoms;

$R^2$  and  $R^3$  are each independently hydrogen or a group as defined for R and  $R^1$  above; or  $R^1$  and  $R^3$  together form a ring having 5 or more ring members;

n is equal to 1, 2 or 3;

X is substituted or unsubstituted alkylene having from 1 to about 6 carbon atoms; and pharmaceutically acceptable salts thereof.

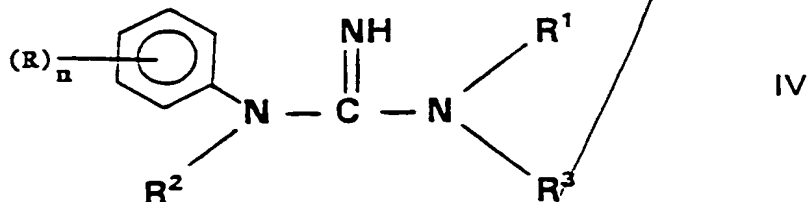
10. A compound of claim 8 selected from the group of:

N-5-acenaphthyl-N'-benzhydrylguanidine;  
N-5-acenaphthyl-N'-benzhydryl-N-methylguanidine;  
N-5-acenaphthyl-N'-benzhydryl-N'-methylguanidine;  
N-5-acenaphthyl-N'-benzhydryl-N,N'-dimethylguanidine;  
N-3-acenaphthyl-N'-benzhydrylguanidine;  
N-3-acenaphthyl-N'-benzhydryl-N-methylguanidine;  
N-3-acenaphthyl-N'-benzhydryl-N'-methylguanidine;  
N-3-acenaphthyl-N'-benzhydryl-N,N'-dimethylguanidine;  
N-(5-acenaphthyl)-N'-[(1-naphthyl)-methyl]guanidine;  
N-(5-acenaphthyl)-N'-[(1-naphthyl)-methyl]-N-methylguanidine;  
N-(5-acenaphthyl)-N'-[(1-naphthyl)-methyl]-N'-methylguanidine;  
N-(5-acenaphthyl)-N'-[(1-naphthyl)-methyl]-N,N'-dimethylguanidine;  
N-(5-acenaphthyl)-N'-(1-methyl-2-phenoxyethyl)guanidine;  
N-(5-acenaphthyl)-N'-(1-methyl-2-phenoxyethyl)-N-methylguanidine;  
N-(5-acenaphthyl)-N'-(1-methyl-2-phenoxyethyl)-N'-methylguanidine;  
N-(5-acenaphthyl)-N'-(1-methyl-2-phenoxyethyl)-N,N'-dimethylguanidine;  
N-(5-acenaphthyl)-N'-(1-methyl-2-(4-chlorophenyl)ethyl)guanidine;  
N-(5-acenaphthyl)-N'-(1-methyl-2-(4-chlorophenyl)ethyl)-N-methylguanidine;



N-(5-acenaphthyl)-N'-(1-methyl-2-(4-chlorophenyl)ethyl)-N'-methylguanidine;  
N-(5-acenaphthyl)-N'-(1-methyl-2-(4-chlorophenyl)ethyl)-N,N'-dimethylguanidine;  
N-(5-acenaphthyl)-N'-(1,2-diphenylethyl)guanidine;  
N-(5-acenaphthyl)-N'-(1,2-diphenylethyl)-N-methylguanidine;  
N-(5-acenaphthyl)-N'-(1,2-diphenylethyl)-N'-methylguanidine;  
N-(5-acenaphthyl)-N'-(1,2-diphenylethyl)-N,N'-dimethylguanidine;  
N-(5-acenaphthyl)-N'-(3-phenylpropyl)guanidine;  
N-(5-acenaphthyl)-N'-(3-phenylpropyl)-N-methylguanidine;  
N-(5-acenaphthyl)-N'-(2-methyl-2-phenylethyl)-N'-methylguanidine;  
N,N'-(*sec*-butylphenyl)-N'-(2-phenoxyethyl)guanidine;  
N,N'-(*sec*-butylphenyl)-N'-(2-phenoxyethyl)-N-methylguanidine;  
N,N'-(*sec*-butylphenyl)-N'-(2-phenoxyethyl)-N'-methylguanidine;  
N,N'-(*sec*-butylphenyl)-N'-(2-phenoxyethyl)-N,N'-dimethylguanidine;  
N-(5-acenaphthyl)-N'-((4-*tert*-butylphenyl)-(4-*sec*-butylphenyl)-methyl)guanidine;  
N-(5-acenaphthyl)-N'-((4-*tert*-butylphenyl)-(4-*sec*-butylphenyl)-methyl)-N-methylguanidine;  
N-(5-acenaphthyl)-N'-((4-*tert*-butylphenyl)-(4-*sec*-butylphenyl)-methyl)-N'-methylguanidine;  
N-(5-acenaphthyl)-N'-((4-*tert*-butylphenyl)-(4-*sec*-butylphenyl)-methyl)-N,N'-dimethylguanidine;  
N-(4-butoxyphenyl)-N,N'-bis(4-*tert*-butylbenzyl)guanidine;  
N-(4-butoxyphenyl)-N,N'-bis(4-*tert*-butylbenzyl)-N-methylguanidine;  
N-(4-butoxyphenyl)-N,N'-bis(4-*tert*-butylbenzyl)-N'-methylguanidine;  
N-(4-butoxyphenyl)-N,N'-bis(4-*tert*-butylbenzyl)-N,N'-dimethylguanidine;  
and pharmaceutically acceptable salts of said compounds.

11. A compound having the following Formula IV:



wherein

each R is independently halo, hydroxy, amino, nitro, substituted or unsubstituted alkyl having from 3 to about 10 carbon atoms, substituted or unsubstituted alkoxy, substituted or unsubstituted aryloxy, substituted or unsubstituted aralkoxy, substituted or unsubstituted aminoalkyl, substituted or unsubstituted alkylthio, substituted or unsubstituted alkylsulfinyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted alkenyl having 3 to about 10 carbon atoms, or substituted or unsubstituted alkynyl having 3 to about 10 carbon atoms, at least one R group is a meta or para substituent;

n is an integer of from 1 to 5;

R<sup>1</sup> is substituted or unsubstituted alkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkoxy having from 1 to about 20 carbon atoms, substituted or unsubstituted aminoalkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted aryloxy having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylthio having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfinyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfonyl having 1 to about 20 carbon atoms, substituted or unsubstituted carbocyclic aryl having at least 5 ring atoms, substituted or unsubstituted aralkyl having at least 5 ring atoms, or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having 1 to 3 rings, 3 to 8 ring members in each ring and 1 to 3 heteroatoms;

R<sup>2</sup> and R<sup>3</sup> are each independently hydrogen or a group as defined R<sup>1</sup> above; or R<sup>2</sup> and R<sup>3</sup> are taken together to form a substituted or unsubstituted alkylene linkage of from 2 to about 6 carbon atoms; and wherein said compound exhibits high inhibition of glutamate release; and pharmaceutically acceptable salts thereof.

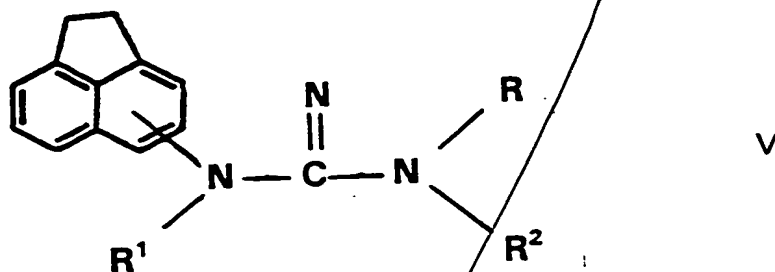
12. A compound of claim 11 selected from the group of:

N,N'-di-(4-*sec*-butylphenyl)guanidine;  
N,N'-di-(4-*sec*-butylphenyl)-N-methylguanidine;  
N,N'-di-(4-*sec*-butylphenyl)-N,N'-dimethylguanidine;  
N-(2-naphthyl)-N'-(4-*isopropyl*phenyl)guanidine;  
N-(2-naphthyl)-N'-(4-*isopropyl*phenyl)-N-methylguanidine;  
N-(2-naphthyl)-N'-(4-*isopropyl*phenyl)-N'-methylguanidine;  
N-(2-naphthyl)-N'-(4-*isopropyl*phenyl)-N,N'-dimethylguanidine;  
N,N'-bis(4-*tert*-butylphenyl)guanidine;  
N,N'-bis(4-*tert*-butylphenyl)-N-methylguanidine;  
N,N'-bis(4-*tert*-butylphenyl)-N'-methylguanidine;  
N,N'-bis(4-*tert*-butylphenyl)-N,N'-dimethylguanidine;  
N-(4-*sec*-butylphenyl)-N'-(2,3,4-trichlorophenyl)guanidine;  
N-(4-*sec*-butylphenyl)-N'-(2,3,4-trichlorophenyl)-N-methylguanidine;  
N-(4-*sec*-butylphenyl)-N'-(2,3,4-trichlorophenyl)-N'-methylguanidine;  
N-(4-*sec*-butylphenyl)-N'-(2,3,4-trichlorophenyl)-N,N'-dimethylguanidine;  
N-(4-methoxy-1-naphthyl)-N'-(2,3,4-trichlorophenyl)guanidine;  
N-(4-methoxy-1-naphthyl)-N'-(2,3,4-trichlorophenyl)-N-methylguanidine;  
N-(4-methoxy-1-naphthyl)-N'-(2,3,4-trichlorophenyl)-N'-methylguanidine;  
N-(4-methoxy-1-naphthyl)-N'-(2,3,4-trichlorophenyl)-N,N'-dimethylguanidine;  
N,N'-bis-(4-*sec*-butylphenyl)-2-iminopyrimidazolidine;  
N,N'-bis(3-biphenyl)guanidine;  
N,N'-bis(3-biphenyl)-N-methylguanidine;  
N,N'-bis(3-biphenyl)-N'-methylguanidine;

N,N'-di-(4-sec-butylphenyl)guanidine;  
N,N'-di-(4-sec-butylphenyl)-N-methylguanidine;  
N,N'-di-(4-sec-butylphenyl)-N,N'-dimethylguanidine;  
N-(2-naphthyl)-N'-(4-isopropylphenyl)guanidine;  
N-(2-naphthyl)-N'-(4-isopropylphenyl)-N-methylguanidine;  
N-(2-naphthyl)-N'-(4-isopropylphenyl)-N'-methylguanidine;  
N-(2-naphthyl)-N'-(4-isopropylphenyl)-N,N'-dimethylguanidine;  
N,N'-bis(4-tert-butylphenyl)guanidine;  
N,N'-bis(4-tert-butylphenyl)-N-methylguanidine;  
N,N'-bis(4-tert-butylphenyl)-N'-methylguanidine;  
N,N'-bis(4-tert-butylphenyl)-N,N'-dimethylguanidine;  
N-(4-sec-butylphenyl)-N'-(2,3,4-trichlorophenyl)guanidine;  
N-(4-sec-butylphenyl)-N'-(2,3,4-trichlorophenyl)-N-methylguanidine;  
N-(4-sec-butylphenyl)-N'-(2,3,4-trichlorophenyl)-N'-methylguanidine;  
N-(4-sec-butylphenyl)-N'-(2,3,4-trichlorophenyl)-N,N'-dimethylguanidine;  
N-(4-methoxy-1-naphthyl)-N'-(2,3,4-trichlorophenyl)guanidine;  
N-(4-methoxy-1-naphthyl)-N'-(2,3,4-trichlorophenyl)-N-methylguanidine;  
N-(4-methoxy-1-naphthyl)-N'-(2,3,4-trichlorophenyl)-N'-methylguanidine;  
N-(4-methoxy-1-naphthyl)-N'-(2,3,4-trichlorophenyl)-N,N'-dimethylguanidine;  
N,N'-bis-(4-sec-butylphenyl)-2-iminopyrimidazolidine;  
N,N'-bis(3-biphenyl)guanidine;  
N,N'-bis(3-biphenyl)-N-methylguanidine;  
N,N'-bis(3-biphenyl)-N'-methylguanidine;  
N,N'-bis(3-biphenyl)-N,N'-dimethylguanidine;

N,N'-di-(3-*tert*-butylphenyl)guanidine;  
N,N'-di-(3-*tert*-butylphenyl)-N-methylguanidine;  
N,N'-di-(3-*tert*-butylphenyl)-N'-methylguanidine;  
N,N'-di-(3-*tert*-butylphenyl)-N,N'-dimethylguanidine;  
N,N'-bis-(4-methoxy-1-naphthyl)guanidine;  
N,N'-bis-(4-methoxy-1-naphthyl)-N-methylguanidine;  
N,N'-bis-(4-methoxy-1-naphthyl)-N'-methylguanidine;  
N,N'-bis-(4-methoxy-1-naphthyl)-N,N'-dimethylguanidine;  
N,N'-bis-(3-*sec*-butylphenyl)guanidine;  
N,N'-bis-(3-*sec*-butylphenyl)-N-methylguanidine;  
N,N'-bis-(3-*sec*-butylphenyl)-N'-methylguanidine;  
N,N'-bis-(3-*sec*-butylphenyl)-N,N'-methylguanidine;  
N,N'-bis(4-*n*-butylphenyl)-N-methylguanidine;  
N,N'-bis(4-*n*-butylphenyl)-N'-methylguanidine;  
N,N'-bis(4-*n*-butylphenyl)-N,N'-dimethylguanidine;  
N,N'-(*sec*-butylphenyl)-N'-(*n*-pentyl)guanidine;  
N,N'-bis(3-benzyloxyphenyl)guanidine;  
N,N'-bis(3-benzyloxyphenyl)-N-methylguanidine;  
N,N'-bis(3-benzyloxyphenyl)-N,N'-dimethylguanidine;  
N,N'-bis(4-benzyloxyphenyl)guanidine;  
N,N'-bis(4-benzyloxyphenyl)-N-methylguanidine;  
N,N'-bis(4-benzyloxyphenyl)-N,N'-dimethylguanidine;  
N-(3-benzyloxyphenyl)-N'-(4-benzyloxyphenyl)guanidine;  
N-(3-benzyloxyphenyl)-N'-(4-benzyloxyphenyl)-N-methylguanidine;  
N-(3-benzyloxyphenyl)-N'-(4-benzyloxyphenyl)-N'-methylguanidine;  
N-(3-benzyloxyphenyl)-N'-(4-benzyloxyphenyl)-N,N'-dimethylguanidine;  
and pharmaceutically acceptable salts of said compounds.

13. A compound of the following Formula V:



wherein:

R is substituted or unsubstituted tetrahydroquinoliny, indoliny or piperonyl;

R<sup>1</sup> and R<sup>2</sup> are each independently hydrogen, substituted or unsubstituted alkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkoxy having from 1 to about 20 carbon atoms, substituted or unsubstituted aminoalkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylthio having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfinyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfonyl having from 1 to about 20 carbon atoms, substituted or unsubstituted carbocyclic aryl having at least 5 ring atoms, substituted or unsubstituted aralkyl having at least 5 ring atoms, or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having 1 to 3 rings, 3 to 8 ring members in each ring and 1 to 3 heteroatoms;

and pharmaceutically acceptable salts thereof.

14. A compound of claim 13 selected from the group of:

N-(5-acenaphthyl)-N'-(1,2,3,4-tetrahydroquinoliny)guanidine;  
N-(5-acenaphthyl)-N'-(1,2,3,4-tetrahydroquinoliny)-N-methylguanidine;  
N-(5-acenaphthyl)-N'-(1,2,3,4-tetrahydroquinoliny)-N'-methylguanidine;

N-(5-acenaphthyl)-N'-(1,2,3,4-tetrahydroquinoliny)-N,N'-dimethylguanidine;  
N-(3-acenaphthyl)-N'-(indoliny)guanidine;  
N-(3-acenaphthyl)-N'-(indoliny)-N-methylguanidine;  
N-(3-acenaphthyl)-N'-(indoliny)-N'-methylguanidine;  
N-(3-acenaphthyl)-N'-(indoliny)-N,N'-methylguanidine;  
N-(5-acenaphthyl)-N'-(piperonyl)guanidine;  
N-(5-acenaphthyl)-N'-(piperonyl)-N-methylguanidine;  
N-(5-acenaphthyl)-N'-(piperonyl)-N'-methylguanidine;  
N-(5-acenaphthyl)-N'-(piperonyl)-N,N'-dimethylguanidine;  
and pharmaceutically acceptable salts of such compounds.

15. A compound of claims selected from the group of:

N-(3-*sec*-butylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-*tert*-butylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(3-pentoxyphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(5-acenaphthyl)-N-(4-benzyloxybenzyl)guanidine;  
N-(4-*sec*-butylphenyl)-N-(4-benzyloxybenzyl)guanidine;  
N-(4-benzyloxyphenyl)-N-(4-benzyloxybenzyl)guanidine;  
N-(5-acenaphthyl)-N-(3-benzyloxybenzyl)guanidine;  
N-(4-isopropylphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(4-benzyloxyphenyl)-N-(4-*tert*-butylbenzyl)guanidine;  
N-(4-hexylphenyl)-N-(4-hexylbenzyl)guanidine;  
N-(4-*sec*-butylphenyl)-N-(4-*t*-butylbenzyl)-N'-pyrrolidinyguanidine;  
N-(4-*sec*-butylphenyl)-N-(4-*t*-butylbenzyl)-N'-(4-thiomorpholiny)guanidine;  
N-(4-*sec*-butylphenyl)-N-(4-*tert*-butylbenzyl)-N'-piperidinyguanidine;  
N-(4-*sec*-butylphenyl)-N-(4-*tert*-butylbenzyl)-N'-(4-morpholiny)guanidine;  
N-(4-*sec*-butylphenyl)-N-(4-*tert*-butylbenzyl)-N'-(4-propylpiperidiny)guanidine;  
N-(4-butoxyphenyl)-N-(4-*tert*-butylbenzyl)-N'-(4-piperidiny)guanidine;  
N-(4-*sec*-butylphenyl)-N-(4-*tert*-butylbenzyl)-N'-(4-benzylpiperidiny)guanidine;

N-(4-benzyloxyphenyl)-N-(4-*tert*-butylbenzyl)-N'-(4-morpholinyl)guanidine;  
N-(4-*sec*-butylphenyl)-N-(4-*tert*-butylbenzyl)-N'-(1,2,3,4-tetrahydroisoquinolinyl)guanidine;  
N-(3-butoxy-4-methoxyphenyl)-N-(4-*tert*-butylbenzyl)-N'-(4-morpholinyl)guanidine;  
N-(4-*sec*-butylphenyl)-N-(4-*tert*-butylbenzyl)-N'-(3,5-dimethyl-4-morpholinyl)guanidine;  
N-(4-*tert*-butylphenyl)-N-(4-*tert*-butylbenzyl)-N'-(4-*sec*-butylphenyl)-N'-(methyl)guanidine;  
N-(4-*sec*-butylphenyl)-N-(4-*tert*-butylbenzyl)-N'-(4-*sec*-butylphenyl)-N'-(methyl)guanidine;  
N-(4-*sec*-butylphenyl)-N-(4-*tert*-butylbenzyl)-N'-(phenyl)guanidine;  
N-(4-*sec*-butylphenyl)-N-(4-*tert*-butylbenzyl)-N'-(4-chlorophenyl)guanidine;  
N-(4-butoxyphenyl)-N-(4-*tert*-butylbenzyl)-N'-(phenyl)guanidine;  
N-(4-*sec*-butylphenyl)-N-(4-*tert*-butylbenzyl)-N'-(phenyl)-N'-methylguanidine;  
N-(4-*sec*-butylphenyl)-N-(4-*tert*-butylbenzyl)-N'-(3,4-dichlorophenyl)guanidine;  
N-(4-hexylphenyl)-N-(4-hexylbenzyl)-N'-phenylguanidine;  
N-(4-*sec*-butylphenyl)-N-(4-*tert*-butylbenzyl)-N'-(4-benzyloxyphenyl)guanidine;  
N,N'-bis-(4-*tert*-butylphenyl)-N,N'-dimethylguanidine  
N-(4-benzyloxyphenyl)-N'-(4-*tert*-butylphenyl)guanidine;  
N,N'-bis-(3-(1'-methyl-2'-phenyl)ethyl)guanidine;  
N-methyl-N-4-benzyloxyphenyl-N'-(4-*tert*-butylphenyl)guanidine;  
N,N'-bis-(4-hexylphenyl)guanidine;  
N-(3-(1-(4'-ethoxy)benzyl)phenethyl)-N'-(4-*tert*-butylphenyl)guanidine;  
N-(4-benzyloxyphenyl)-N'-methyl-N'-(4-*tert*-butylphenyl)guanidine;  
N-(3-(4-*tert*-butylbenzyloxy)phenyl)-N'-(4-*tert*-butylphenyl)guanidine;  
N-(3-(1'-benzylbutyl)phenyl)-N'-(4-*tert*-butylphenyl)guanidine;  
N,N'-bis-(4-butylphenyl)-N-methylguanidine;  
N,N'-bis-(4-*tert*-butylphenyl)-N,N'-dimethylguanidine;

N-(3-naphthylmethyleneoxyphenyl)-N'-(4-*tert*-butylphenyl)guanidine;  
N-(4-benzyloxyphenyl)-N'-(4-butylphenyl)guanidine;  
N,N'-bis-(4-butylphenyl)-N-butylguanidine;  
N-3-(benzyloxymethyl)phenyl-N'-(4-*tert*-butylphenyl)guanidine;  
N-(3,4-bis-butylloxyphenyl)-N'-(4-*tert*-butylphenyl)guanidine;  
N-(3-benzyloxy)phenyl-N'-(4-*tert*-butylphenyl)guanidine;  
N,N'-bis-(3-butoxy-4-methoxy)phenylguanidine;  
N-(4-benzyloxyphenyl)-N-methyl-N'-(4-butylphenyl)guanidine;  
N,N'-bis-(6-tetralinyl)guanidine;  
N-(6-tetralinyl)-N'-(4-*tert*-butylphenyl)guanidine;  
N-(5-acenaphthyl)-N'-(6-benzothiozoly)guanidine;  
N-(5-acenaphthyl)-N'-(6-N-benzylindoliny)guanidine;  
N-(5-acenaphthyl)-N'-(4-benzo-2,1,3-thiadizaole)guanidine;  
N-(5-acenaphthyl)-N'-[4-(6-methyl-benzothiazole)phenyl]guanidine;  
N-(5-acenaphthyl)-N'-(1-benz[cd]indoliny)guanidine;  
N-(5-acenaphthyl)-N'-(6-benz[cd]indo-2[1H]-one)guanidine;  
N,N'-bis(6-benz[cd]indoliny-2[1H]-one)guanidine;  
N-(4-butoxyphenyl)-N'-(4-chlorophenylethyl)guanidine;  
N-(4-benzyloxyphenyl)-N,N'-diphenylguanidine;  
N-(4-benzyloxyphenyl)-N'-benzyl-N'-phenylguanidine;  
N-(3-benzyloxyphenyl)-N'-(4-thiobenzylphenyl)guanidine;  
N,N'-bis(4-(phenylthio)phenyl)guanidine;  
N,N'-bis(3-(phenylthio)phenyl)guanidine;  
N-(5-acenaphthyl)-N'-(2-phenylethyl)guanidine;  
N-(5-acenaphthyl)-N'-(3-butoxypropyl)guanidine;  
N,N'-bis(2,2-diphenylethyl)guanidine;  
N-(4-butoxyphenyl)-N'-(4-chlorophenylethyl)guanidine;  
N-(4-butoxyphenyl)-N-(4-chlorobenzhydryl)guanidine;  
(5-acenaphthyl)-N'-(phenethyl)-N'-benzylguanidine;  
N-(4-benzyloxyphenyl)-N'-(3-benzyloxyphenyl)-N'-(4-chlorobenzyl)guanidine;  
N,N'-bis(4-benzyloxyphenyl)-N'-methylguanidine;



N-(4-benzyloxyphenyl)-N'-(3-benzyloxyphenyl)-N'-(4-chlorobenzyl)guanidine;  
N-(3-benzyloxyphenyl)-N'-(4-benzyloxyphenyl)-N'-phenylguanidine;  
N-(4-sec-butylphenyl)-N'-(4-isopropoxyphenyl)-N'-phenylguanidine;  
N-(4-benzyloxyphenyl)-N'-(4-benzyloxyphenyl)-N'-phenylguanidine;  
N,N'-bis(3-octyloxyphenyl)guanidine;  
N,N'-bis(4-butoxyphenyl)guanidine;  
N,N'-bis(4-phenoxyphenyl)guanidine;  
N-(3-benzyloxyphenyl)-N'-(4-phenoxyphenyl)guanidine;  
N-(3-benzyloxyphenyl)-N'-(4-phenylazophenyl)guanidine;  
N,N'-bis(3-benzyloxyphenyl)-N'-methylguanidine;  
N-(4-benzyloxyphenyl)-N'-(4-benzyloxyphenyl)-N'-methylguanidine;  
N-(4-butoxyphenyl)-N'-(4-isopropoxyphenyl)guanidine;  
N,N'-bis(4-(1-hydroxybutyl)phenyl)guanidine;  
N-(4-butoxyphenyl)-N'-(3-methoxyphenyl)-N'-phenylguanidine;  
N-(4-secbutylphenyl)-N'-phenyl-N'-(4-(2-isopropoxy)phenyl)guanidine;  
N-(4-n-butoxyphenyl)-N'-(2-(4-chlorophenyl)ethyl)guanidine;  
and pharmaceutically acceptable salts thereof.

16. A method for treating a disorder of the nervous system in which the pathophysiology of the disorder involves excessive or inappropriate release of a neurotransmitter from neuronal cells comprising administering to a mammal exhibiting symptoms of said disorder or susceptible to said disorder an effective amount of a compound of any of the preceding claims.

17. A method for treating nerve cell death comprising administering to a mammal exhibiting symptoms of nerve cell death or susceptible to nerve cell death an effective amount of a compound of any one of ~~claims 1-~~

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Claims 1, 8, 11 or 13.

18. A method for treating a person who has suffered or is suffering from a stroke, or who is susceptible to a stroke, comprising administering to the person an effective amount of a compound of any one of ~~claims 1-15.~~

*claims 1, 8, 11 or 13.*

19. A method of treating a disease of the cardiovascular system comprising administering to a mammal suffering from or susceptible to a cardiovascular disease an effective amount of a compound of any one of ~~claims 1-15.~~

*claims 1, 8, 11, or 13.*

20. A method of modulating the release of excess endogenous neurotransmitters from a subject comprising administering to the subject an effective amount of a compound of any one of ~~claims 1-15.~~

*claims 1, 8, 11 or 13.*

21. A method for treating a disease in which the pathophysiology of the disease involves inappropriate cellular secretion comprising administering to a mammal suffering from or susceptible to said disease an effective amount of a compound of any one of ~~claims 1-15.~~

*claims 1, 8, 11 or 13.*

22. A method for 1) blocking voltage-activated calcium channels of mammalian neuronal cells; 2) blocking voltage-activated sodium channels of mammalian neuronal cells; 3) blocking voltage sensitive calcium channels of mammalian cardiac cells; 4) blocking voltage-activated sodium channels of mammalian cardiac cells; 5) blocking voltage-activated calcium channels of mammalian smooth or skeletal muscle cells; or 6) blocking voltage-activated sodium channels of mammalian smooth or skeletal muscle cells, comprising administering to said cells an effective amount of a compound of any one of ~~claims 1-15.~~

*claims 1, 8, 11 or 13.*

23. A method for diagnosing a selected disease the pathophysiology of which involves ion-channel excitation or activity comprising administering to a mammal suffering from the disease a

A

detection effective amount of a labeled compound of any one of claims 1-15. claims 1, 8, 11 or 13.

24. A pharmaceutical composition comprising a therapeutically effective amount of one or more compounds of any one of claims 1-15 and a pharmaceutically acceptable carrier. claim 1, 8, 11 or 13.

A

~~Chapters 1, 8, 11 or 13.~~

add